

## **REMARKS**

In the Final Action dated December 29, 2006, claims 39, 44-46, 51, 56-58, 60-61, 63-64, 67-68, 86, 94 and 100-104 were pending and under consideration. Claims 39, 44-46, 51, 60, 63-64, 67 and 100-104 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Thomson et al. ("Thomson") in view of Brustle et al. ("Brustle"). The remaining claims were rejected as allegedly unpatentable over Thomson in view of Brustle, and further in view of either or both of Ben-Hur and Stemple.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

By way of the instant amendment, claims 39, 51, 56, 60, 61, 67, 86 and 101 have been amended. Claims 46, 58, 63, 64, 68 and 100 have been canceled without prejudice, and claims 105 to 113 have now been added.

More specifically, claim 39 has been amended to further delineate that the undifferentiated pluripotent hES cells are cultured "for 2-3 weeks under adherent conditions". Support for the phrase "2-3 weeks" is found in the specification on page 76, line 10. The phrase "under adherent conditions" is supported by the specification, as it is apparent from all the Examples of the specification that small packed colonies of cells are cultured on substrates under adherent conditions.

Claims 51 and 56 have been amended to delineate that the neural progenitor cells are differentiated into neurons. Support for the recitation "determining an expression of a neuronal cell marker" is found in the instant application on page 81, line 24.

Claims 60 and 61 have been amended to depend from claim 39 and to further delineate that the neuronal progenitor cells are differentiated into astrocytes or oligodendrocytes

New claims 105 to 106 depend from claim 39 and include a step of selection of cells destined to give rise to neural progenitors from the differentiating cell population based on cell morphology. The selection procedure is disclosed, for example, at page 76 of the specification.

New claims 107 and 113 find support in the specification, for example, at pages 81-82.

New claim 108 is supported, for example, at page 76, lines 17-19 of the specification.

New claims 109 and 110 are directed to the culturing of undifferentiated pluripotent hES cells so as to generate differentiating hES cells without a generation of embryoid bodies. These claims are also supported by the specification. For example, the specification discloses, at page 75, lines 18-20, that a prolonged cultivation (4-7 weeks) of the ES cells does not lead to the formation of embryoid bodies. Since the period of time for culturing the ES cells is for 2-3 weeks, as disclosed in page 76 and as presently claimed, it is reasonable to extrapolate from this that the differentiating colonies exemplified on page 76 are not embryoid bodies and do not contain embryoid bodies.

New claim 111 finds support in the specification, for example, at page 76, line 9.

It is respectfully submitted that the amendments made to the claims herein are fully supported by the specification and do not introduce new matter.

Turning to the Examiner's rejection of claims 39, 44-46, 51, 60, 63-64, 67 and 100-104 as obvious based on Thomson in view of Brustle, the Examiner alleges that a) Thomson teaches that ES cells are pluripotent and therefore have the potential to differentiate into neuronal progenitor cells; and b) Brustle teach techniques that employ the same factors as those employed

in Applicants' methods and that were used for culturing mouse ES cells into glial cells, which may inherently contain neuronal cells.

In response, Applicants respectfully submit that the culturing method of Brustle is not identical with the methods as presently claimed. For example, in contrast to amended claim 39, Brustle does not culture cells under adherent conditions for 2-3 weeks.

In addition, regarding the Examiner's contention that the differentiated cell population of Brustle may inherently comprise some neuronal cells, Applicants submit that the fact that a certain characteristic may be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (emphasis added). Moreover, even assuming, *pro arguendo*, that the differentiated cell population of Brustle inherently contained some neuronal cells, Brustle would not have provided any motivation, or any reason, for those skilled in the art to determine an expression of a neuronal cell marker, as presently recited in amended claims 51 and 56. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown. *Id.*, at 1534.

Furthermore, the culturing conditions and techniques of the present invention do not allow for the generation of embryoid bodies. Indeed, in sharp contrast to the method of Brustle which requires the generation of embryoid bodies, the present specification and the claims (claims 109 and 110, for example) state that no embryoid bodies are generated during the procedure.

Therefore, Applicants respectfully submit that the culturing conditions, as presently recited in the claims, are not taught or suggested in Brustle. Thus, the fundamental premise for combining Brustle with Thomson by the Examiner no longer exists. Accordingly, it is

respectfully submitted that the methods, as presently claimed, are not obvious over Thomson in view of Brustle. The *prima facie* case of obviousness is fully rebutted and withdrawal of the rejection is therefore respectfully requested.

Applicants further respectfully submit that because the combined teachings of Thomson and Brustle do not render the presently claimed invention obvious, the two references cannot provide a basis for the remaining obviousness rejections when used in combination with Stemple et al and Ben-Hur et al. Withdrawal of all the §103 rejections is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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